



# Appropriate Treatment of Common Infections in Primary Care

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“Antimicrobial stewardship is defined as a formalized program that provides advice, consent, and institutional guidance on appropriate selection, dosing, route and duration of antimicrobial usage.”

# Outline

- Urinary Infections
  - Appropriate Selection of Antibiotics
  - Appropriate Duration of Antibiotics
- Respiratory Infections
  - Big Data can improve outcomes

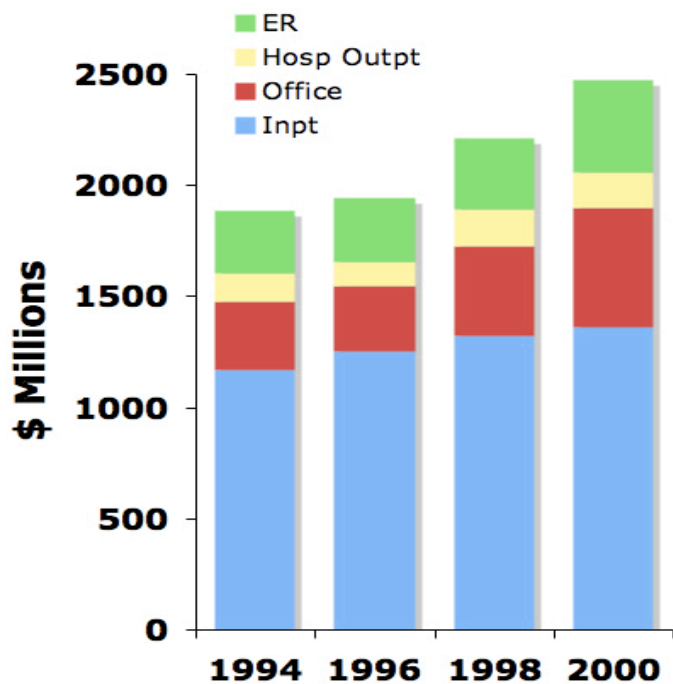
# UTI

Among 20-40 yo women, 35% have had a UTI

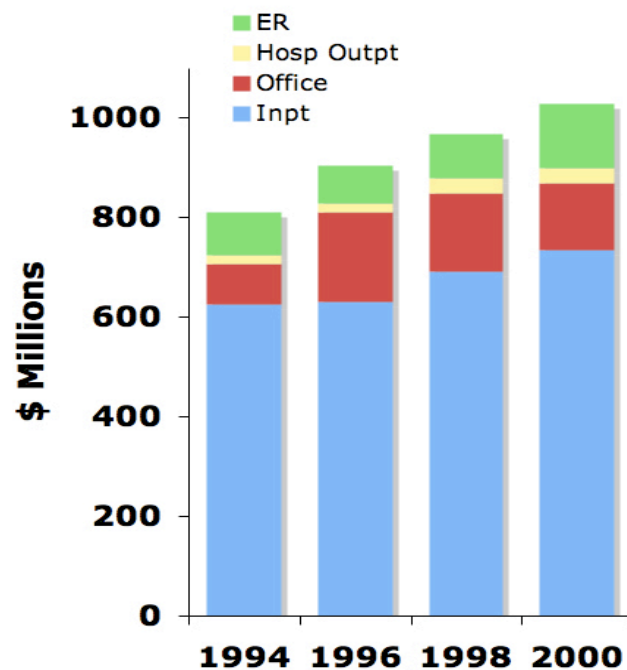
- 1.8 - 6.1 days of symptoms
- 0.6 - 1.2 days of missed work or classes
- 0.4 - 0.6 days in bed

# US Expenditures

## Women (\$2.5B)

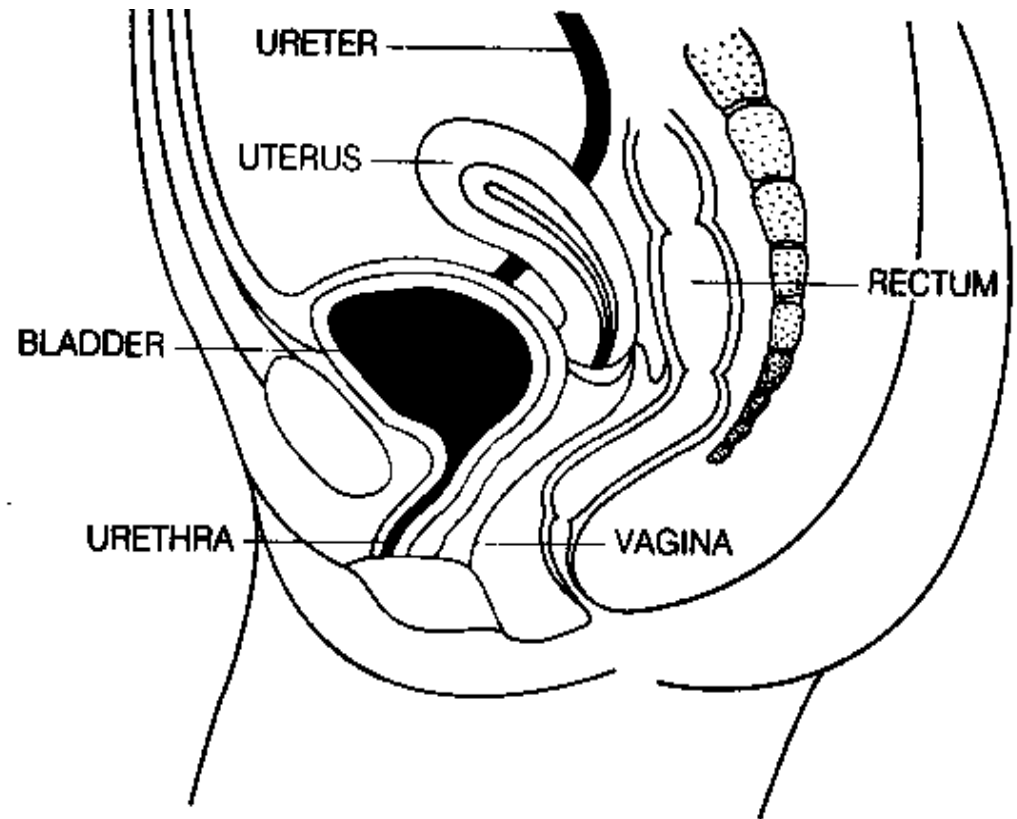
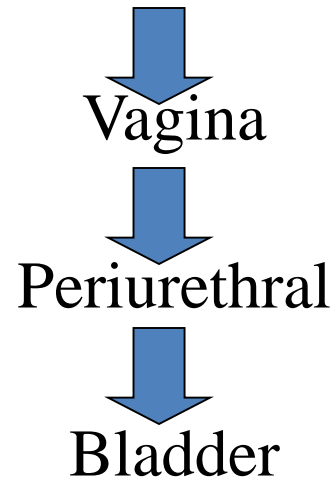


## Men (\$1B)



# UTI's: Pathogenesis

Colonization of GI tract



# Case #1

22 year old female presents with a chief complaint of **burning** when she pees. She reports **frequency** and **urgency**. No fever, no systemic symptoms. No CVA tenderness.

# Cystitis

Symptoms from a Lower Tract Infection Result from Inflammation of the Bladder and Urethra

- Frequency, Urgency
- Pain
- Burning (“Ardor”)
- Hematuria



# Case #1

A: 22 year old female with cystitis, but no systemic symptoms. Physical Exam is unremarkable. UA is positive for LE and Nitrites, Umicro shows 15 WBC and 7 RBC.

P: No Culture Needed, Treat Empirically

**Trimethoprim/Sulfamethoxazole po BID x 3 Days**

- Wait ... Did this Guy Just Say Trimethoprim/Sulfamethoxazole?
- ...Is He Crazy?

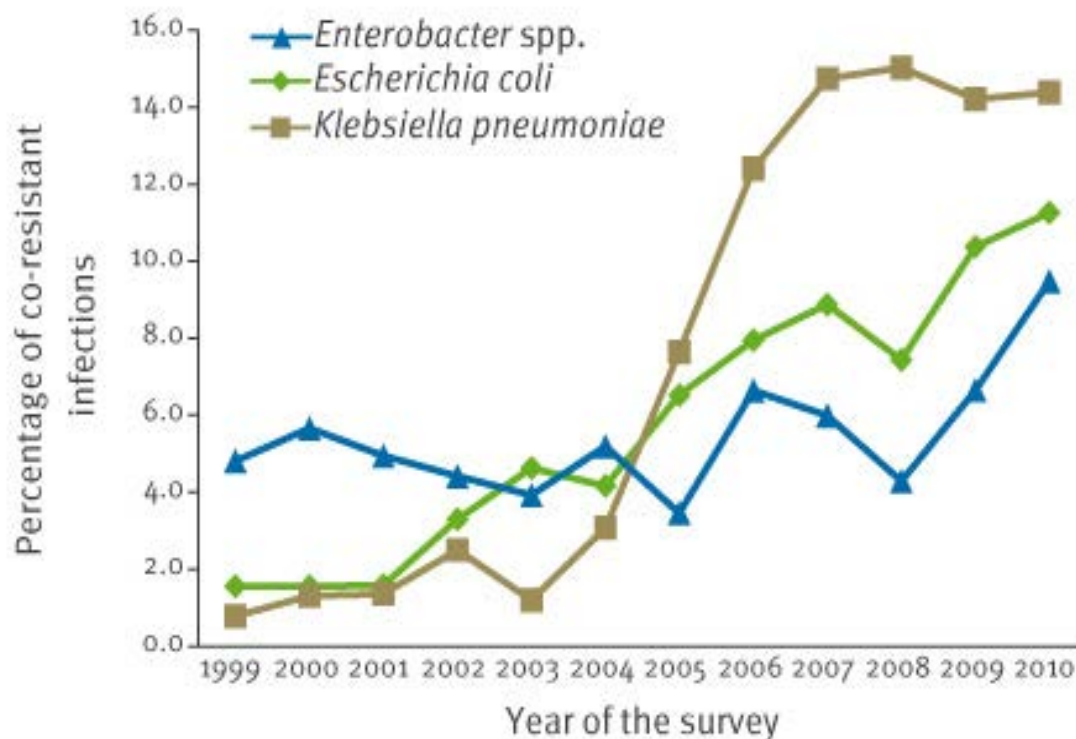
# IDSA Guidelines: Uncomplicated UTIs

- First Line Therapy
  - **TMP-SMX DS BID x 3 Days**
  - **Nitrofurantoin 100mg BID x 5 Days**
  - Fosfomycin 3 grams PO x 1 dose
  - Pivmecillinam – Not available in US
- Second Line Therapy
  - **Fluoroquinolones** -- Collateral Damage
  - $\beta$ -lactams -- Less likely to be effective

# Fluroquinolone Resistance is Here

**FIGURE 4**

Annual rates of *Enterobacteriaceae* co-resistant to fluoroquinolones and third-generation cephalosporins, Spain, 1999–2010



# FDA Black Box Warning

The FDA first added a Boxed Warning to fluoroquinolones in [July 2008](#) for the increased risk of tendinitis and tendon rupture. In February 2011, the risk of worsening symptoms for those with myasthenia gravis was added to the Boxed Warning. In [August 2013](#), the agency required updates to the labels to describe the potential for irreversible peripheral neuropathy (serious nerve damage).

In November 2015, an [FDA Advisory Committee](#) discussed the risks and benefits of fluoroquinolones for the treatment of acute bacterial sinusitis, acute bacterial exacerbation of chronic bronchitis and uncomplicated urinary tract infections based on new safety information. The new information focused on two or more side effects occurring at the same time and causing the potential for irreversible impairment. The advisory committee concluded that the serious risks associated with the use of fluoroquinolones for these types of uncomplicated infections generally outweighed the benefits for patients with other treatment options.

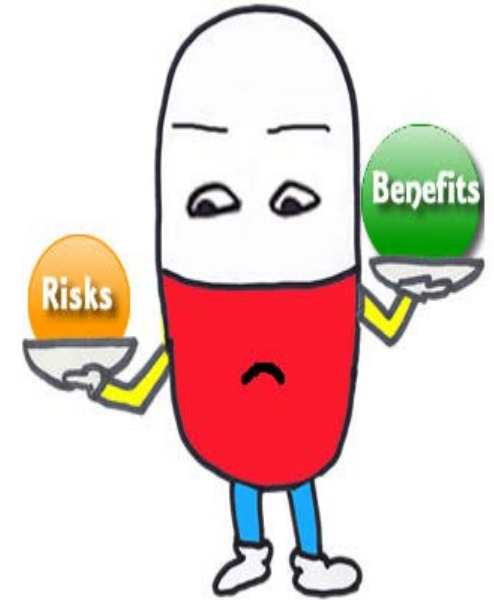
Today's action also follows a May 12, 2016, [drug safety communication](#) advising that fluoroquinolones should be reserved for these conditions only when there are [no other options](#) available due to potentially permanent, disabling side effects occurring together. The drug safety communication also announced the required labeling updates to reflect this new safety information.

# FDA Black Box Warning For

- Sinusitis
- COPD Exacerbation
- Uncomplicated Urinary Tract Infections

# FQ Serious Adverse Effects

- Photosensitivity
- Hypersensitivity
- **QT prolongation**
- Peripheral neuropathy
- **Tendinitis or tendon rupture**
- **CNS effects**
- Myasthenia gravis exacerbation



# Examining Fluoroquinolone Use through the Lens of Antimicrobial Stewardship

James A. McKinnell, M. D.



## Case #2

22 year old female reports five days of frequency, urgency, and burning. Today, she reports back pain, fever, and emesis.

# Pyelonephritis

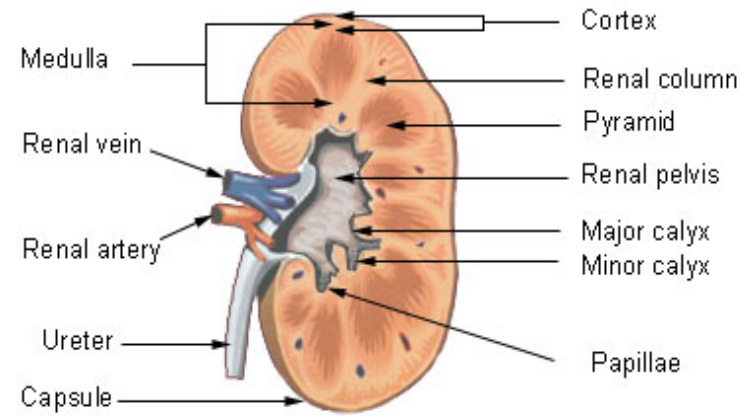
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Fevers, Chills, Nausea

Costovertebral-Angle Tenderness

Suppurative  
Necrosis of the  
Kidney

**Frontal section through the Kidney**



# Case #2

A: 22 year old female with pyelonephritis evidenced by cystitis with systemic symptoms, CVA tenderness, positive LE and Nitrites.

P: Obtain Urine Culture and Initiate Empiric Antibiotics while awaiting Urine Culture Results

**Trimethoprim/Sulfamethoxazole po BID x 7 Days**

- Wait ... Did this Guy Just Say Seven Days for Pyelonephritis?
- ...Is He Crazy?

One Third of What You Learned in Medical School is  
Wrong...

**The Trick is Figuring Out Which Third**

# PYELONEPHRITIS

## 5-7 DAYS

- **Several RCTs 5-7 days equal to 10-14 days**
- **Short course effective despite diabetes and GNB bacteremia**

Jernelius et al. Acta Med Scand 1988;223:469-77; de Gier R, Karperien A, Bouter K, et al. 1995. Int J Antimicrob Agents 6:27-30; Talan DA, Stamm WE, Hooton TM, et al. 2000 JAMA 283:1583-90; Sandberg et al. 2012 Lancet 380:484-90; Peterson et al. 2008 Urology 71:17-22; Klausner et al. 2007. Current medical research and opinion 23:2637-45.

# Community Associated Pneumonia

## 3-5 Days

- **Multiple RCT showing 3-5 days NI to 7 - 10 days**
- **Includes pts with PORT IV and V**  
**(Uranga et al. JAMA IM)**
- **Reduced emergence of resistance**

Singh et al. Am J Respir Crit Care Med 2000;162:505-11; Dunbar et al. Clin Infect Dis 2003;37:752-60; Zhao X et al. Diagn Microbiol Infect Dis 2014;80:141-7; Pakistan Multicentre Amoxicillin Short Course Therapy pneumonia study group. Lancet 2002;360:835-41; Greenberg et al. The Pediatric infectious disease journal 2014;33:136-42; Dunbar et al. Current medical research and opinion 2004;20:555-63; el Moussaoui et al. Bmj 2006;332:1355; Uranga et al. JAMA IM 2016 176:1257-65.

# CELLULITIS/ABSCESS

## 5 DAYS

- **Numerous trials show that 5-7 equal to 10-14 days**
- **Drainage of abscess is key**
- **When you drain and abscess, treat with antibiotics.**

Hepburn 2004 Arch Int Med 164:1669-74; Prokocimer 2013 JAMA 309:559-69; Moran 2014 Lancet ID 14:696-705.



# AECB/COPD

## 3-5 DAYS

- **Dozens of Studies**
- **Meta-analysis show that 3-5 days of therapy equal to 7 or more days.**

El Moussaoui 2008 Thorax 68:415-22

# Short Course Therapy!!!!

Diagnosis	Short (d)	Long (d)	Result
CAP	3 or 5	7, 8, or 10	Equal
HAP	7	10-15	Equal
VAP	8	15	Equal
Pyelo	7 or 5	14 or 10	Equal
Intra-abd	4	10	Equal
AECB	$\leq 5$	$\geq 7$	Equal
Cellulitis	5-6	10	Equal
Osteo	42	84	Equal

# Colonization or Infection?

One of the most dangerous results in modern medicine is a positive urine culture.



A positive culture is not the same as an infection  
The diagnosis of a UTI requires Symptoms!



Hello Doctor, I'm sorry  
to bother you...

“Doctor, I’m calling you to let you know that the Urine Culture for HR Is Positive.”

“Read me the sensitivities.”

“Levofloxacin 500 mg po daily x 10 days.”



**Table 2. Prevalence of asymptomatic bacteriuria in selected populations.**

Population	Prevalence, %	Reference
Healthy, premenopausal women	1.0–5.0	[31]
Pregnant women	1.9–9.5	[31]
Postmenopausal women aged 50–70 years	2.8–8.6	[31]
Diabetic patients		
Women	9.0–27	[32]
Men	0.7–11	[32]
Elderly persons in the community <sup>a</sup>		
Women	10.8–16	[31]
Men	3.6–19	[31]
Elderly persons in a long-term care facility		
Women	25–50	[27]
Men	15–40	[27]
Patients with spinal cord injuries		
Intermittent catheter use	23–89	[33]
Sphincterotomy and condom catheter in place	57	[34]
Patients undergoing hemodialysis	28	[28]
Patients with indwelling catheter use		
Short-term	9–23	[35]
Long-term	100	[22]

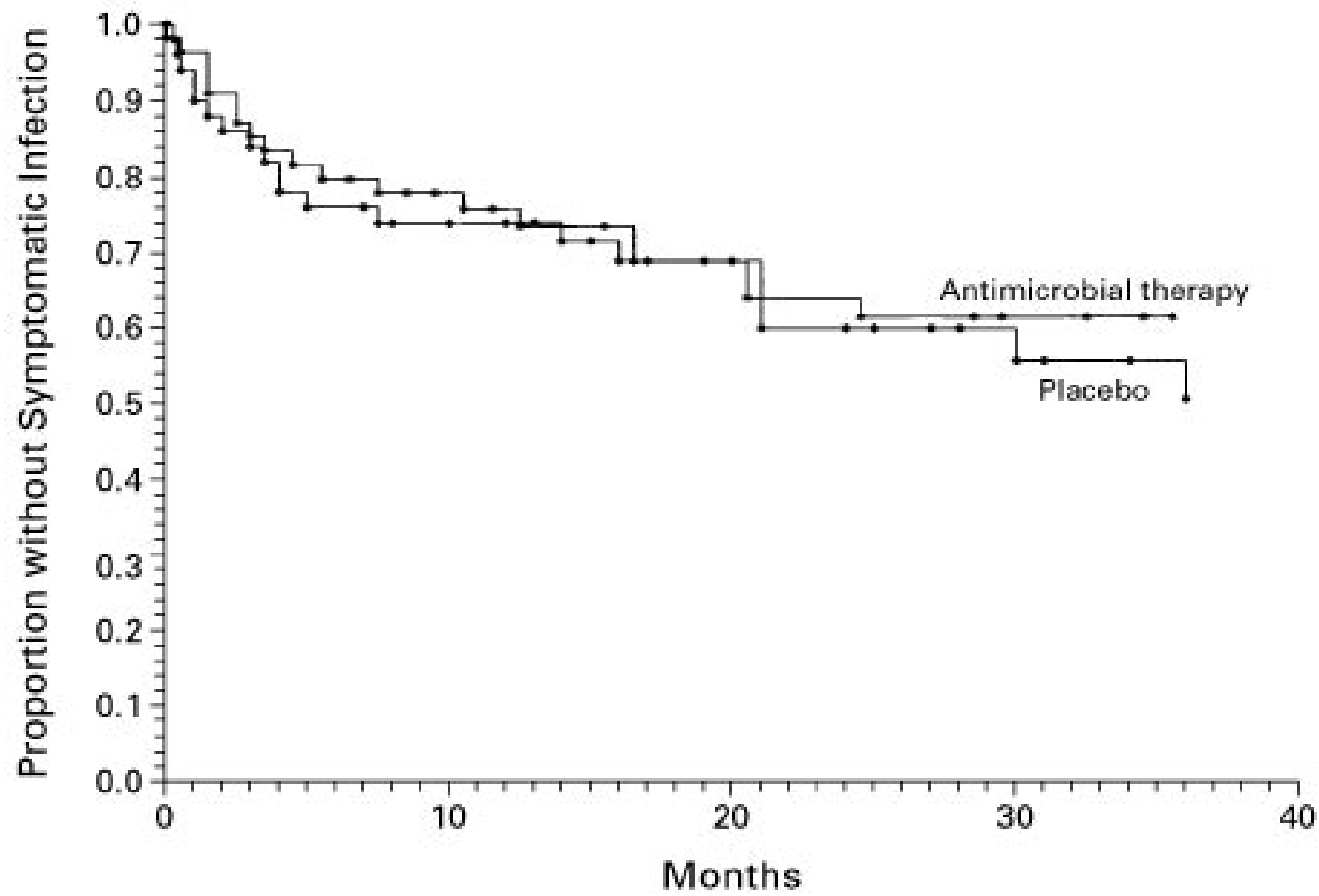
<sup>a</sup> Age,  $\geq 70$  years.

# Prospective Randomized Studies

## Treatment vs. No Treatment ASB

Authors	Subjects	Intervention	Outcome
Nicolle LE, et al. NEJM 1983;309:1420-5	Men, NH, median age 80	Treated 16 Not treated 20 Duration 2 years	No difference mortality or infectious morbidity 2 groups
Nicolle LE, et al. Am J Med 1987;83:27-33	Women, NH, median age 83	Treated 26 Not treated 24 Duration 1 year	No difference mortality/GU morbidity. <b>Increase drug reactions and AB resistance treated group.</b>
Abrutyn E, et al. Ann Intern Med 1994;120:827-33	Women, ambulatory and NH Mean age 82	Treated 192 Not treated 166 Duration 8 years	No survival benefit from treatment
Ouslander JG Ann Intern Med 1995;122:749-54	Women and men NH Mean age 85	Treated 33 Not treated 38 Duration 4 weeks	No difference chronic urinary incontinence

**Proportion of Women with Diabetes Who Remained Free of Symptomatic Urinary Tract Infection, According to Whether They Received Antimicrobial Therapy or Placebo at Enrollment.**





# Outline

- Urinary Infections
  - Appropriate Selection of Antibiotics
  - Appropriate Duration of Antibiotics

# Resources for Antibiotic Selection

- Sanford Guide
- Project Aware (California Medical Foundation)
- ID Physicians

(Yes, I'll take questions afterwards)

“Does Education Alone Change Provider Behavior?”

## Research

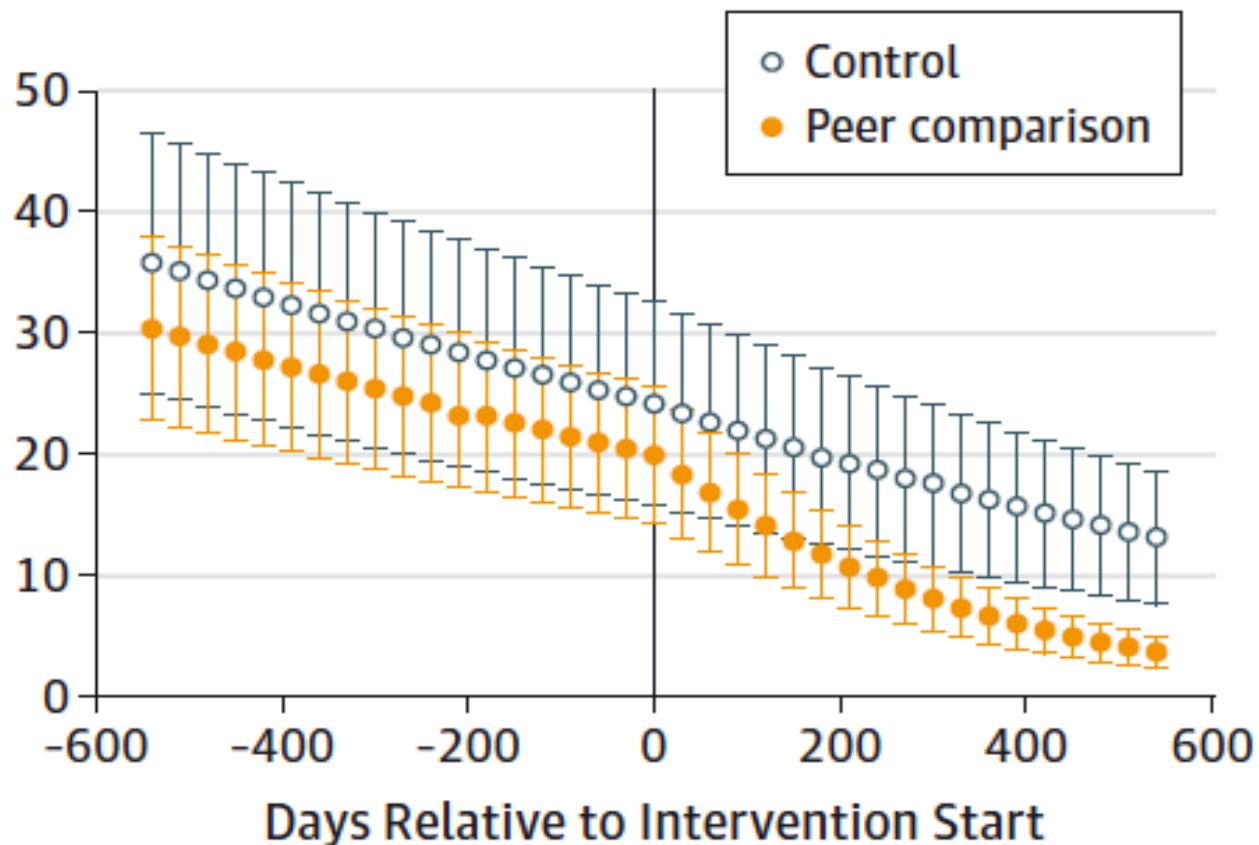
## Original Investigation

# Effect of Behavioral Interventions on Inappropriate Antibiotic Prescribing Among Primary Care Practices A Randomized Clinical Trial

Daniella Meeker, PhD; Jeffrey A. Linder, MD, MPH; Craig R. Fox, PhD; Mark W. Friedberg, MD, MPP;  
Stephen D. Persell, MD, MPH; Noah J. Goldstein, PhD; Tara K. Knight, PhD; Joel W. Hay, PhD; Jason N. Doctor, PhD

# Behavioral Interventions are Key!!!

**B** Peer comparison



# Bill

**48 year old male with no past medical history complaining of persistent cough x 2 weeks. Still able to perform ADLs, though cough is “annoying” and “Going on Forever”. “I need antibiotics”**

T:98.6 P:116/62 R: 14 S:92%

CXR is Clear

- No Acute Distress
- Scattered Rhonchi

# Acute URI - Bronchitis

- Cough --- by definition - 5 days  
1-3 week duration, mean 18 days
- Viruses represent about 60% of Acute Bronchitis
- Bacteria represent about 6% of Acute Bronchitis
- Sputum production can be seen with viral infections

- “CDC, American College of Physicians, National Health Services of the UK, all recommend against treating acute bronchitis with antibiotics.”
- Among otherwise healthy individuals, antibiotics have not demonstrated any consistent benefit in the symptomatology or natural history of acute bronchitis.
- Healthcare Effectiveness Data and Information Set for NCQA and National Quality Forum quality measure.
- **In Real World Clinical Practice, Bronchitis and Cough can be fairly complex and may actually be a wobbler for when you might need antibiotics.**



# Acute URI - Do Not Treat

- Early in the Course of a Clear Viral Syndrome
- Post Nasal Drip - Allergic Rhinitis or Viral
- Sore Throat - Viral
- Undiagnosed Asthma - 65% of patients with two or more episodes of bronchitis in a 5 year period have mild asthma that has simply not been diagnosed
- CHF, PE, GERD

# Acute URI - Bronchitis --- TREAT

- Acute Exacerbation of COPD - Absolutely Treat!
- Fever, Tachycardia, Tachypnea -Admit to Hospital?
- Post viral Complication
- Non-Healthy Adults: Immunosuppressed Patients, *Streptococcus* infection, mycobacterial infections, cystic fibrosis, diseases of the spleen, Crohn's disease, bacterial pneumonia- Maybe Treat

# LADPH TAP OUT Program

- Initiative from the LAC DPH to help support Antimicrobial Stewardship Activities
- Specifically targeting inappropriate prescribing for Bronchitis, acute URI

# LA DPH TAP OUT Program

EHR extracted for encounters with URI ICD-10 codes

Encounters excluded if have comorbidity, immunosuppressed

Overall and individual rates calculated

For Example:

- Bronchitis (J20)
- URI (J069)
- Influenza (J10)
- Nasopharyngitis (J00)
- Allergic Rhinitis (J30)
- Cough (R05)

For Example:

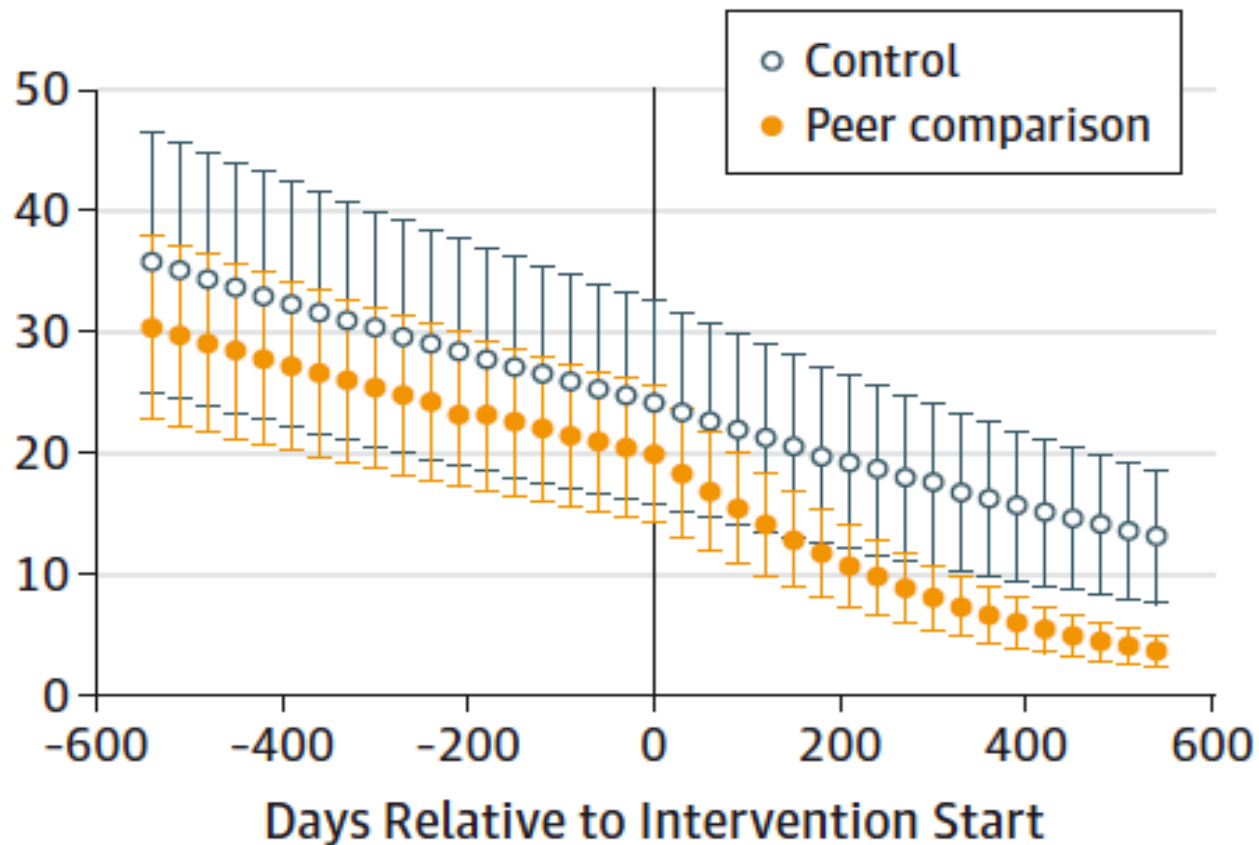
- COPD (J44)
- Immunosuppressed
- *Streptococcus* (B95)
- Disease of spleen (D73)
- Bacterial pneumonia (J15)
- Crohn's disease (K50)

# Baseline results

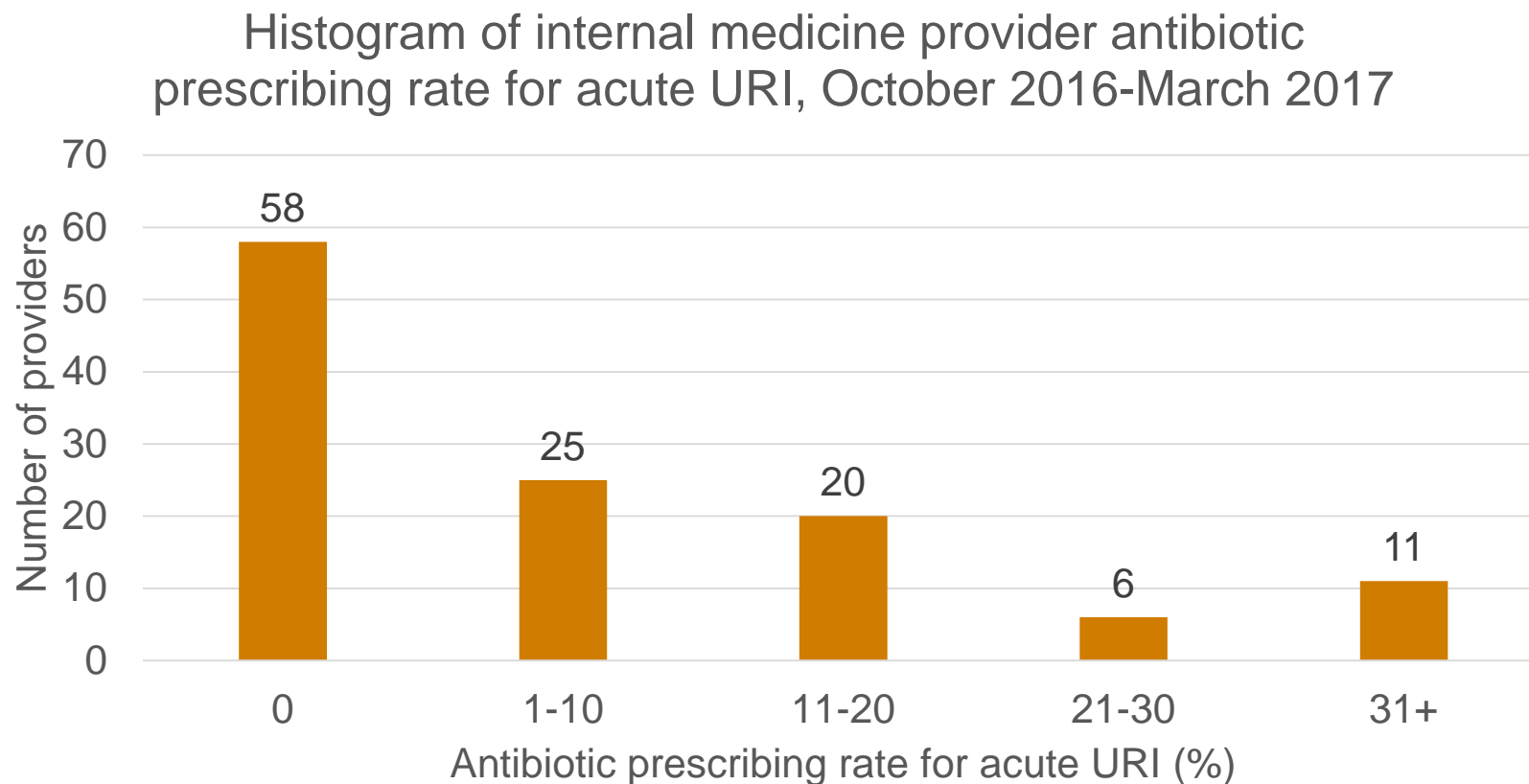
- October 1, 2016 through March 31, 2017
- 4,651 Total number encounters
  - Cough (2488)
  - Acute upper respiratory infection, unspecified (382)
  - Allergic rhinitis, unspecified (380)
- 615 Encounters (13%) Resulted in an Antibiotic Prescription
  - Cough (487)
  - Bronchitis (89)
  - Acute upper respiratory infection, unspecified (46)

# Baseline Utilization was Low!!!

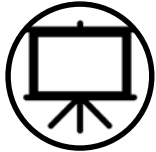
**B** Peer comparison



# Histogram of internal medicine provider antibiotic prescribing rate for acute URI, October 2016-March 2017



# LA County DPH Tap Out Program Components



Public commitment posters  
in waiting areas



Communication skills  
training



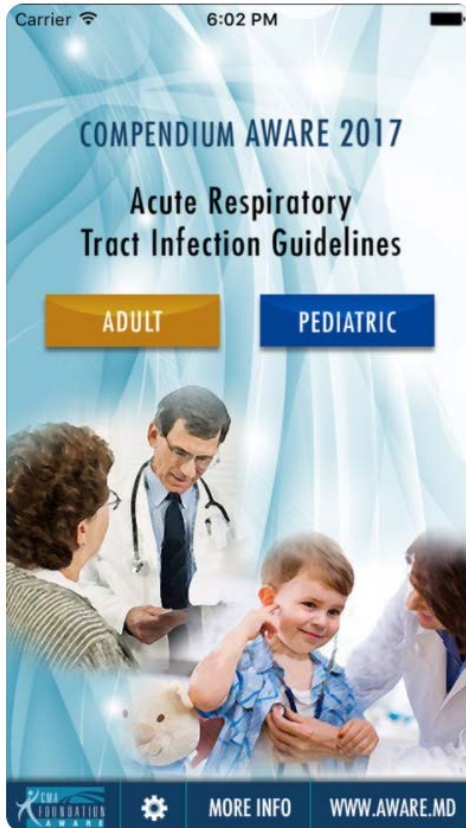
Clinical education on  
treatment guidelines



Monthly peer comparison  
reports emailed to each  
provider



# Commitment Poster's and Guidelines



## When do you need antibiotics?

### You **NEED** antibiotics if you have ...

- ✓ Whooping Cough
- ✓ Strep Throat
- ✓ Urinary Tract Infection

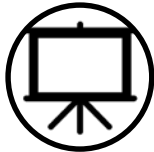
### You **DON'T** need antibiotics if you have ...

- ✗ Cold/Runny Nose
- ✗ Flu
- ✗ Bronchitis/Chest Cold
- ✗ Sore Throat
- ✗ Fluid in the Middle Ear

Antibiotics only fight infections caused by bacteria and will not relieve symptoms caused by a viral infection, such as a cold or flu. Unneeded antibiotics can cause diarrhea, rashes or yeast infections and make future infections more difficult to treat.

As your healthcare provider, we are dedicated to practicing safe and effective antibiotic use. Ask us about alternative treatment plans.

# Tap Out Program Components



Public commitment posters  
in waiting areas



Communication skills  
training



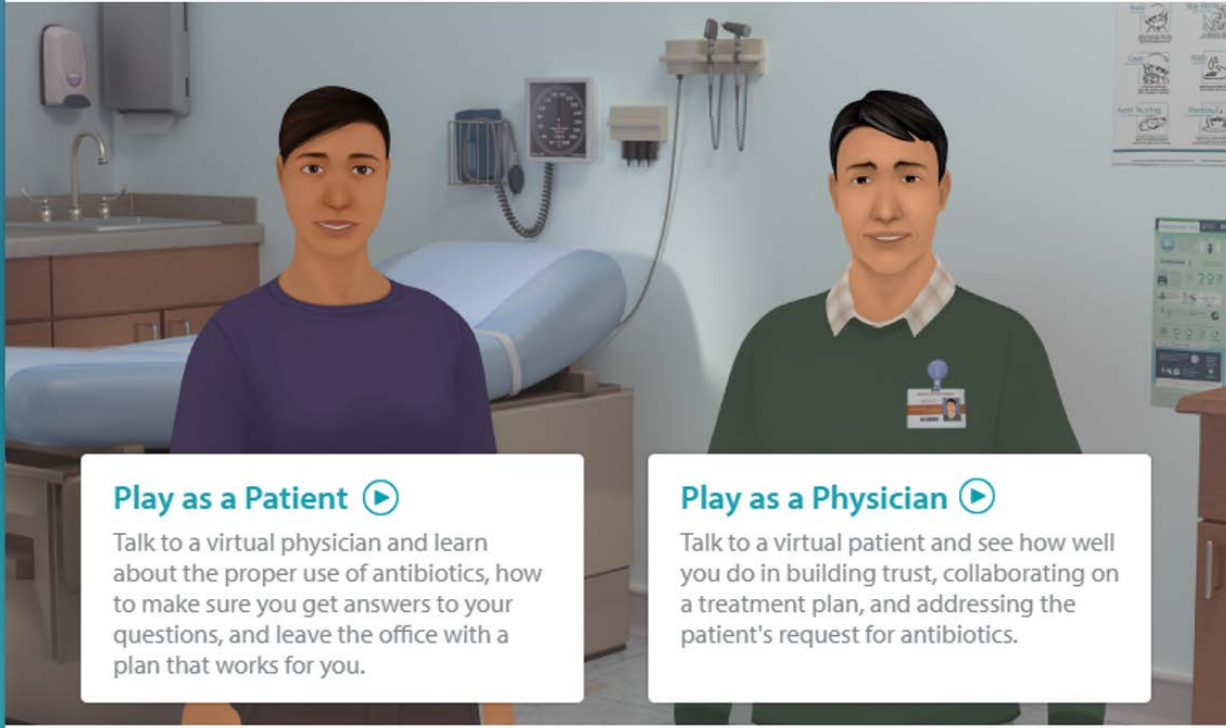
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# Communication Skills Training

**The Primary Care Office Visit: Antibiotics**



**Play as a Patient** ▶

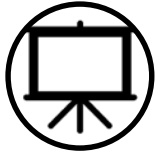
Talk to a virtual physician and learn about the proper use of antibiotics, how to make sure you get answers to your questions, and leave the office with a plan that works for you.

**Play as a Physician** ▶

Talk to a virtual patient and see how well you do in building trust, collaborating on a treatment plan, and addressing the patient's request for antibiotics.

Created by Kognito with the generous support of the Robert Wood Johnson Foundation

# Tap Out Program Components



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# Peer Comparison

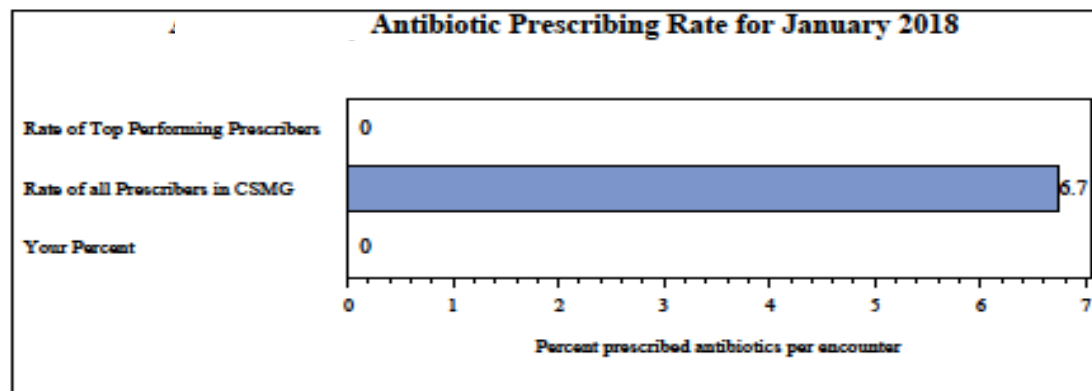
February 16, 2018;

Dear ,

Below you will find data regarding your antibiotic prescribing practices for acute viral respiratory infections. You are a top performer for the period of January 2018, compared to your peers in Cedars-Sinai Medical Group primary care.

Based on your recent activity, you wrote 0 prescriptions out of 23 acute upper respiratory infection cases that did not warrant antibiotics.

These data are based on documentation in CS-Link.

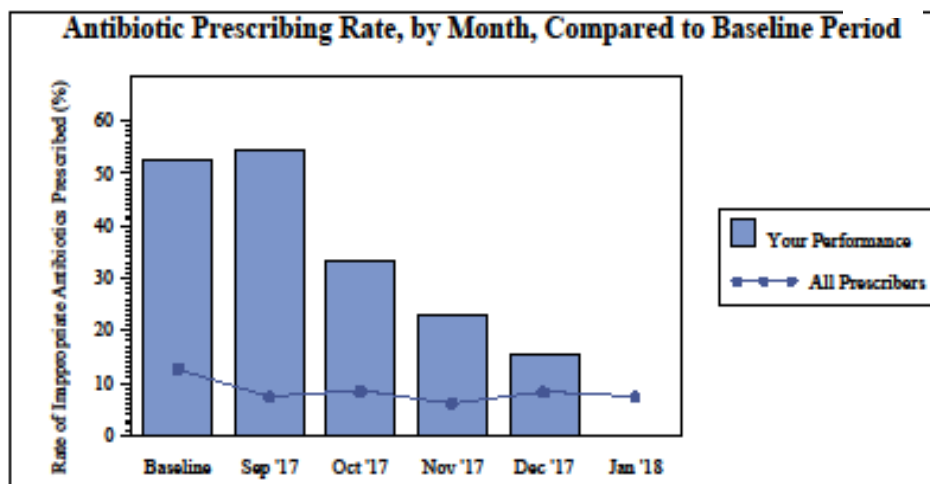


Your prescribing rate depends on the number of antibiotics dispensed for eligible patients with visits to your practice. Eligible patients are those who have a diagnosis of a respiratory illness that is generally non-bacterial in nature.

- Began sending peer comparison reports in October

# Peer Comparison

The graph below shows how your current performance compares to your performance during the baseline period, which is the entire cold/flu season last year (October 2016 through March 2017). You can also see how your baseline and current performance compare to all primary care prescribers in the Cedars-Sinai Medical Group.

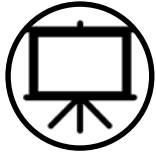


Acute upper respiratory infection treatment guidelines can be found at:  
<http://www.thecmafoundation.org/Portals/0/assets/docs/Physician-Resources/AWARE/compendium-adult-2016-11x17-final-web.pdf?ver=2016-12-14-090913-470>

If you would like to discuss any part of this feedback, please contact Hayden Lowenstein, MD, or Neel Joshi, MD (Co-Chairs, Infection Prevention Committee).

- Began sending peer comparison reports in October

# Tap Out Program Components



Public commitment posters  
in waiting areas



Communication skills  
training

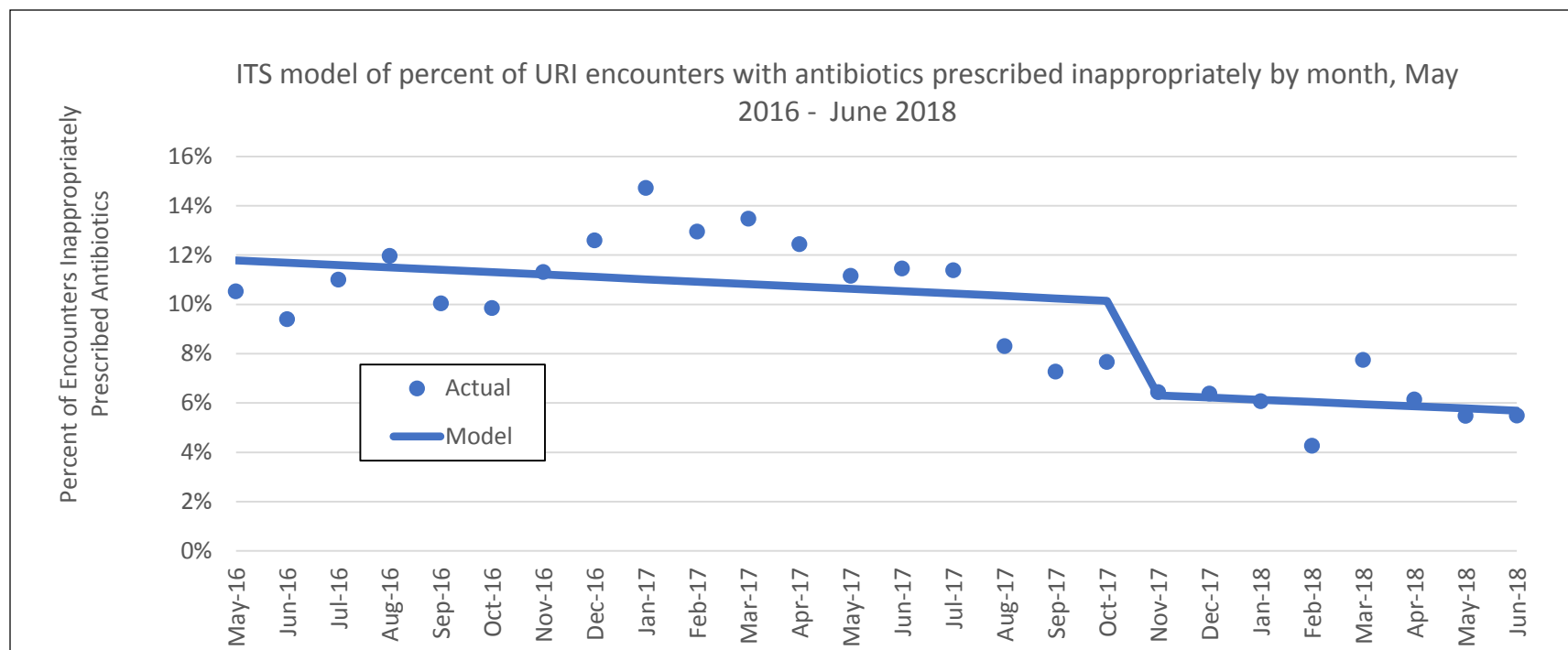


Clinical education on  
treatment guidelines



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# Over 45% Reduction in Inappropriate Use



Baseline (May'16-Oct'17)

Encounters inappropriately prescribed antibiotics of total patient encounters (%)

Intervention (Nov'17-Jun '18)

Encounters inappropriately prescribed antibiotics of total patient encounters (%)

Percent change

	Baseline (May'16-Oct'17) Encounters inappropriately prescribed antibiotics of total patient encounters (%)	Intervention (Nov'17-Jun '18) Encounters inappropriately prescribed antibiotics of total patient encounters (%)	Percent change
Total	1710/15056 (11.36)	658/10947 (6.00)	-47.2%
IM	925/9212 (10.04)	386/6997 (5.52)	-45.0%
UC	785/5844 (13.43)	271/3950 (6.86)	-48.9%



# Public Commitment Poster

- Helpful in communicating to patients  
18/21 (86%)
- Reinforced their commitment to prescribe appropriately  
11/21 (52%)

# Communication Skills Training

- Only 7% completed the online communication skills training.

# In Person Educational Sessions

- Useful in understanding stewardship or reinforcing existing knowledge  
12/21 (55%)
- Enhancing knowledge of antibiotic choice and duration  
7/21 (33%)

# Peer Reports

- Monthly peer comparison reports were useful in understanding their prescribing habits (6.3 out of 10)
- Reactions ranged
  - **Feeling proud of their prescribing rates (45%)**
  - **Realizing the rates could improve (35%)**
  - **Reviewing individual encounters (28%)**
  - **Useless (14%)**

# Value of Antibiotics

Disease	Pre-Antibiotic Death Rate	Death With Antibiotics	Change in Death
Community Pneumonia <sup>1</sup>	~35%	~10%	<b>-25%</b>
Hospital Pneumonia <sup>2</sup>	~60%	~30%	<b>-30%</b>
Heart Infection <sup>3</sup>	~100%	~25%	<b>-75%</b>
Brain Infection <sup>4</sup>	>80%	<20%	<b>-60%</b>
Skin Infection <sup>5</sup>	11%	<0.5%	<b>-10%</b>
<i>By comparison...treatment of myocardial infarction with aspirin or fibrinolytic drugs<sup>6</sup></i>			<b>-3%</b>

<sup>1</sup>IDSA Position Paper '08 Clin Infect Dis 47(S3):S249-65; <sup>2</sup>IDSA/ACCP/ATS/SCCM Position Paper '10 Clin Infect Dis 51(S1):S150-70; <sup>3</sup>Kerr AJ. Subacute Bacterial Endocarditis. Springfield IL: Charles C. Thomas, 1955 & Lancet 1935 226:383-4; <sup>4</sup>Lancet '38 231:733-4 & Waring et al. '48 Am J Med 5:402-18; <sup>5</sup>Spellberg et al. '09 Clin Infect Dis 49:383-91 & Madsen '73 Infection 1:76-81; <sup>6</sup>88 Lancet 2:349-60

Thank you for your time...